REMARKS

Claims 1, 7, 8, and 10, are currently pending in the application. Only claim 1 is in independent form.

The Office Action has held that the previously submitted oath or declaration is defective. A new oath or declaration is attached hereto. Reconsideration of the objection is respectfully requested.

The specification was objected to because it was missing pages 94-99. Enclosed herewith are the missing pages, which pages contain DNA sequence information. Reconsideration of the objection is respectfully requested.

Claim 7 is objected to because the term "lipofectin" is included, it should be read "lipofection" and such a change is shown and made herewith.

The Office Action has held that claim 21 is objected to because if it is not supported by the specification. Claim 21 has been canceled without prejudice thereby rendering the present objection is moot.

Claims 7 and 9 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Office Action has held that claim 7 includes the trademark name "lipofectin." This is a typographical error and it should read "lipofection" and reconsideration of the rejection is respectfully requested.

The Office Action has held that claim 9 is indefinite because it is unclear whether the scope of infusions is intended to include all types of infusions. Claim 9 has been canceled without prejudice thereby rendering the present rejection moot. Reconsideration of the rejection is respectfully requested.

Claim 7 stands rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The Office Action contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The Office Action has held that claim 7 includes the term "lipofectin", which is not supported by the specification. As this is a typographical that has been corrected herewith, reconsideration of the rejection is respectfully requested.

Claims 1, 7-13, 15-18, 20-22, and 24 stand rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for methods of providing a

biologically active moiety *in vivo* by implanting Sertoli cells that have been isolated and modified in a laboratory apparatus so as to express the biologically active moiety in pharmaceutically effective amounts *in vivo* does not reasonably provide enablement for such methods using any other type of naturally immune privileged cells. The claims have been amended to recite that neurotrophic factors are administered. A "trophic factor" is generally defined as any molecule that supports the survival of cells. Nerve growth factors are polypeptides that regulate the proliferation, survival, migration, and differentiation of cells in the nervous system. Most studies have focused on the effect of growth factors on neuronal survival and maintenance; hence the term "neurotrophic factors." By definition, a neurotrophic factor is synthesized by, and released from, target cells of the neurons. It is bound to specific receptors, then internalized and transported by retrograde axonal transport to the cell soma where multiple survival-promoting effects are initiated. The study of these factors began in the 1930s; however, it was 20 years later that a target-derived soluble protein was shown to influence neuronal survival, and was termed "nerve growth factor" (Levi-Montalcini and Hamburger 1953).

Nerve growth factor provided the first molecular basis for the concept of neurotrophic signaling between neurons and their targets; however, recognition of the therapeutic potential of nerve growth factor did not take place until the 1960s (Cohen 1960). Another 20 years passed before the discovery of further nerve growth factors in the 1980s. These discoveries included isolation of brain-derived neurotrophic factor (Barde et al 1982), localization of fibroblast growth factor in neurons of the brain (Pettmann et al 1986), and cloning of brain-derived neurotrophic factor (Leibrock et al 1989). Besides nerve growth factor, a family of nerve growth factor-related polypeptides called "neurotrophins" have been identified along with their specific receptors: neurotrophin-3 (Maisonpierre et al 1990), neurotrophin-4 (Hallbook et al 1991), and neurotrophin-6 (Gotz et al 1994). Other recent discoveries in this area include cloning of human ciliary neurotrophic factor (Lam et al 1991) and isolation of rat glial cell line-derived neurotrophic factor (Lin et al 1993).

Growth factors, termed "cytokines," have also been found to modulate neuronal processes and are sometimes referred to as neuropoietic cytokines or, simply, neurokines. Originally, cytokines were considered to be derived solely from the cells of the immune system, but now they are known to be produced by the cells of the central nervous system also. Therefore, the term "neurotrophic factors" will be used in a broad sense to cover all neurotrophins (nerve growth factor and brain-derived neurotrophic factor), growth factors,

and other substances that promote survival and repair of the cells of the nervous system. A practical classification of neurotrophic factors is as follows: nerve growth factors; brain-derived neurotrophic factor; neurotrophins: NT-3, NT-4/5, NT-6; neuropoietic cytokines (neurokines); ciliary neurotrophic factor family; leukemia inhibitory factor and cholinergic differentiation factor; cardiotrophin-1; oncostatin M; growth promoter activity factor; tumor necrosis factor; ligands for epidermal growth factor receptor family (p185erbB2, p160erbB3,p180erbB4); neuregulins; Neu differentiation factor or heregulin; acetylcholine receptor-inducing activity; glial growth factors; fibroblast growth factors; transforming growth factors: (transforming growth factor-beta); glial cell line-derived neurotrophic factor; neurturin (homologue of glial cell line-derived neurotrophic factor); persephin (identical to glial cell line-derived neurotrophic factor and neurturin); osteogenic Protein-1; bone morphogenetic proteins and growth differentiation factors; insulin-like growth factors; platelet-derived growth factor; hepatocyte growth factor; neurotransmitters and neuromodulators; serine protease inhibitors: protease nexin-1; hedgehog family of inducing proteins; proteins involved in synapse formation: agrin, laminin 2, and ARIA (ACh-inducing activity); neuroimmunophilins; pigment epithelium-derived factor; activity-dependent neurotrophic factor; and angiogenesis growth factor. Therefore, there is support in the specification as originally filed for the claims as amended and reconsideration of the rejection is respectfully requested.

Claims 12, 13, 15, 18, 20-22, and 24 stand 35 U.S.C. § 102(b) as being anticipated by the Builder, et al. patent. As these claims have been canceled without prejudice this renders the present rejection moot and reconsideration of the rejection is respectfully requested.

Claims 12, 16, and 17 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over the Builder, et al. patent in view of the Lipshultz, et al. reference. As these claims have been canceled without prejudice this renders the present rejection moot and reconsideration of the rejection is respectfully requested.

The remaining dependent claims not specifically discussed herein are ultimately dependent upon the independent claims. References as applied against these dependent claims do not make up for the deficiencies of those references as discussed above. The prior art references do not disclose the characterizing features of the independent claims discussed above. Hence, it is respectfully submitted that all of the pending claims are patentable over the prior art.

In view of the present amendment and foregoing remarks, reconsideration of the rejections and advancement of the case to issue are respectfully requested.

The Commissioner is authorized to charge any fee or credit any overpayment in connection with this communication to our Deposit Account No. 11-1449.

Respectfully submitted,

KOHN & ASSOCIATES, PLLC

Amy E. Rinaldo
Registration No. 45,791
30500 Northwestern Highway
Suite 410
Farmington Hills, Michigan 48334
(248) 539-5050

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Marie M. Lally